

REMARKS

Applicant appreciates acknowledgement of the RCE request and entry of the Amendment. Applicant also appreciates the acknowledgement that the discussion presented in the Amendment accompanying the RCE is clear. The title of the invention has been modified to be more descriptive.

The following comments relate to the rejections under 35 U.S.C. § 112.

Taking, first, the rejection under 35 U.S.C. § 112, paragraph 2, it is believed that the amendments to the claims address this rejection. As to claim 39, subparagraph (b) has been amended to indicate that measuring the intensity of the detectable light results in determining the activity of the protein as proportional to this intensity. With respect to claim 44, antecedent basis has been supplied for “concentration” in subparagraph (b). “The” intensity of light has been used throughout since light inherently has intensity, so that antecedent basis is found in reference to light *per se*. “The emitted” has been changed to “any emitted.” In claim 44, also, “the” has been removed as a modifier of activity; however, CETP inherently has activity so the modifier “the” would nevertheless have been appropriate. It is believed that the amendments to the claims are completely responsive to the rejection under 35 U.S.C. § 112, paragraph 2, and this basis for rejection may be withdrawn.

The rejection under 35 U.S.C. § 112, first paragraph, is apparently based on both written description and enablement. Reconsideration of this basis for rejection is requested. As explained beginning on page 9 of the specification, the apparent level of CETP in a sample, as compared to its actual level, may be distorted by the level of acceptor protein – high levels of acceptor protein may

make it appear that higher levels of CETP are present. See, for example, pages 9-10, bridging paragraph. In particular, it is stated at the end of the paragraph,

The patient's plasma with high LDL cholesterol will appear to have a high CETP activity when in fact the apparently high activity is due to the greater number of LDL particles available to accept transfer of the NBD-CE or other fluorescent cholesterol.

The present invention seeks to remedy this distortion by supplying a normalizing color development reaction as set forth in the last full paragraph on page 10. As noted in that paragraph, the concentration of cholesterol ester (CE), triglycerides (TG) or phospholipids (PL) are indicative of the LDL concentration. Thus, there is full support for measuring the activity in a sample where an undetermined concentration of acceptor is present. As set forth in this same paragraph, this is done by supplying reagents that generate a color from CE or TG (representative of acceptor) to have a quenching effect on the fluorescent label – *i.e.*, that creates a quenching effect on the labeled CE as set forth in page 10, last paragraph. As now clarified in the claim, the intensity of the detectable emitted light is proportional to the activity of CETP in the sample independent of the concentration of acceptor.

Taking the comments made by the Office in order, the Office is correct that the claims are directed to an assay with a normalizer component. As to there being a chemical reaction cascade, this may or may not be the case. One way to generate a color that will quench the fluorescent label is to carry out the reactions on pages 11-12, bridging paragraph; or pages 12-13, bridging paragraph. However, this is not the only way to effect a quenching of the light emitted from the released labeled CE or labeled substance generally (as in claim 39); turbidity could also be generated. The particular colorimetric reaction or turbidity-generating reaction is within the skill of the art to select. The invention lies in providing a means to normalize the emitted light from the labeled substance

released from the donor in proportion to the concentration of acceptor present not in the specific method chosen.

The Office goes on to state that on page 10, second paragraph, last line, it is not seen that CETP mass is measured and applicant is puzzled as to why this comment is made. The sentence referred to simply states that the activity measured will not reflect the actual amount of CETP, because of failure to normalize the results according to the level of acceptor present.

Applicant agrees that the sentence cited on page 11 may be confusing but it is not inconsistent with the invention. It is simply trying to say that the normalizing system generates a color where the color interferes with the signal from the released labeled substance. Applicant is unclear as to in what manner the example on page 12 is insufficiently detailed to follow. Considerable detail is given in the last paragraph with regard to color development in response to one of the surrogate markers for acceptor, TG. As to there being no data or results, applicant is unaware of any rule that such results must be provided. Thus, the conclusory statement that one of skill could not perform the claimed invention by following the teachings of the specification appears unsupported.

Respectfully, the description in the specification supports the present claims as it describes the nature of the problem to be solved (pages 9-10, bridging paragraph) describes the method of solving the problem (page 10, last paragraph) and gives an example to illustrate the solution in terms of the measurement of CETP on page 11, first full paragraph. Illustrative color generating reactions (and they are only illustrative, not limiting) are given on pages 12-13.

Accordingly, applicant asserts that the application as filed provides adequate support for the current claims and requests that the rejection under 35 U.S.C. § 112, paragraph 1, be withdrawn.

Conclusion

In light of the amendments responsive to the rejection under 35 U.S.C. § 112, paragraph 2, and in light of the identification of the appropriate sections of the specification in support of the present claims, applicant believes that the pending claims, claims 39-46 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 527832000300.

Respectfully submitted,

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